CLAIMS

We claim:

1. A targeting construct comprising:
   (a) a first polynucleotide sequence homologous to at least a first portion of an A2D2 calcium channel subunit gene;
   (b) a second polynucleotide sequence homologous to at least a second portion of the A2D2 calcium channel subunit gene; and
   (c) a selectable marker.
2. A method of producing a targeting construct, the method comprising:
   (a) providing a first polynucleotide sequence homologous to at least a first portion of an A2D2 calcium channel subunit gene;
   (b) providing a second polynucleotide sequence homologous to at least a second portion of the A2D2 calcium channel subunit gene;
   (c) providing a selectable marker; and
   (d) inserting the first sequence, second sequence, and selectable marker into a vector to produce the targeting construct.
3. A cell comprising a disruption in an A2D2 calcium channel subunit gene.
4. The cell of claim 3, wherein the cell is a murine cell.
5. The cell of claim 4, wherein the murine cell is an embryonic stem cell.
6. A non-human transgenic animal comprising a disruption in an A2D2 calcium channel subunit gene.
7. The non-human transgenic animal of claim 6, wherein the transgenic animal is a mouse.
8. A cell derived from the transgenic mouse of claim 7.
9. A method of producing a transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, the method comprising:
   (a) introducing the targeting construct of claim 1 into a cell;
   (b) introducing the cell into a blastocyst;
   (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
   (d) breeding the chimeric mouse to produce the transgenic mouse.

10. A method of identifying an agent that modulates the expression or function of an A2D2 calcium channel subunit gene, the method comprising:

    (a) providing a non-human transgenic animal comprising a disruption in the A2D2 calcium channel subunit gene;

    (b) administering the agent to the non-human transgenic animal; and

    (c) determining whether the expression or function of the disrupted A2D2 calcium channel subunit gene in the non-human transgenic animal is modulated.

11. A method of identifying an agent that modulates the expression or function of an A2D2 calcium channel subunit gene, the method comprising:

    (a) providing a cell comprising a disruption in the A2D2 calcium channel subunit gene;

    (b) contacting the cell with the agent; and

    (c) determining whether the expression or function of the A2D2 calcium channel subunit gene is modulated.

12. The method of claim 11, wherein the cell is derived from the non-human transgenic animal of claim 6.

13. An agent identified by the method of claim 10 or claim 11.

14. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein there is no significant expression of the A2D2 calcium channel subunit gene in the transgenic mouse.

15. A cell derived from the transgenic mouse of claim 14.

16. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits, relative to a wild-type mouse, a behavioral abnormality.

17. The transgenic mouse of claim 16, wherein the behavioral abnormality is selected from the group consisting of ataxia, reduced activity, reduced responsiveness, weakness and freezing.

18. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits a locomotive abnormality, relative to a wild-type control mouse.

19. The transgenic mouse of claim 18, wherein the locomotive abnormality is selected from the group consisting of stumbling, reduced coordination, abnormal gait, tremor, paddling movements and paralysis.
20. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse dies perinatally.
21. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits a growth abnormality, relative to a wild-type control mouse.
22. The transgenic mouse of claim 21, wherein the growth abnormality is dwarfism.
23. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits one or more of reduced body size, reduced body weight or reduced body length, relative to a wild-type control mouse.
24. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits reduced weight for one or more of thymus, spleen, liver, kidney or heart, relative to a wild-type control mouse.
25. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits reduced organ weight to body weight ratio for one or more of thymus, spleen or liver, relative to a wild-type control mouse.
26. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse has an abnormal organ selected from the group consisting of thymus, spleen, kidney, liver, lymph node and heart, relative to a wild-type control mouse.
27. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits one or more of thymic atrophy, splenic hypoplasia or lymph node hypoplasia, relative to a wild-type control mouse.
28. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits an abnormality with a body system selected from the group consisting of immune system, digestive system, urinary system and cardiovascular system, relative to a wild-type control mouse.

29. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits a posture abnormality, relative to a wild-type control mouse.
30. The transgenic mouse of claim 29, wherein the posture abnormality is a hunched posture.
31. A transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the transgenic mouse exhibits an eye abnormality, relative to a wild-type control mouse.
32. The transgenic mouse of claim 31, wherein the eye abnormality is reduced eye size.
33. The transgenic mouse of claim 31, wherein the eye abnormality is eye squinting.
34. A method of identifying an agent that ameliorates a phenotype associated with a disruption in an A2D2 calcium channel subunit gene, the method comprising:

    (a) administering an agent to a transgenic mouse comprising a disruption in the A2D2 calcium channel subunit gene; and

    (b) determining whether the agent ameliorates the phenotype, wherein the phenotype comprises one or more of: behavioral abnormality; locomotive abnormality; perinatal lethality; growth abnormality; decreased body size; decreased organ weight; decreased organ:body weight; abnormal thymus, spleen, kidney, liver, lymph node or heart; thymic atrophy; splenic hypoplasia; lymph node hypoplasia; posture abnormality; and eye abnormality.
35. An agent identified by the method of claim 34.
36. An agonist or antagonist of A2D2 calcium channel subunit.
37. Phenotypic data associated with a transgenic mouse comprising a disruption in an A2D2 calcium channel subunit gene, wherein the phenotypic data is in an electronic database.